2200/1634

PATENT #15
B. Webb
5/3/01

Customer Number 22,852
Attorney Docket No. 1147-0142

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Reissue Application of:
U.S. Patent No. 5,750,338

Mark L. Collins et al.

Reissue Serial No.: 09/533,906

Reissue Application Filed: March 8, 2000

For: TARGET AND BACKGROUND CAPTURE METHODS WITH AMPLIFICATION FOR AFFINITY ASSAYS

Group Art Unit: 1655

Examiner: D. Johannsen

REISSUE LITIGATION BOX
Assistant Commissioner for Patents
Washington, DC 20231

Sir:

RESPONSE TO INTERVIEW SUMMARY

The Patent Owner and its representatives wish to express their appreciation to Examiner Johannsen, Examiner Myers, and Special Programs Examiner Tsang for their courtesy and helpful discussion during the interview on January 16, 2001. The Patent Owner's representatives also wish to thank Examiner Johannsen for so quickly providing the Interview Summary the following day. The Patent Owner's representatives also greatly appreciate the Examiners' willingness to consider additional information/arguments with respect to the issues raised during the interview and wish to address the following four points.

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1. Support for Unexpectected Results

The Interview Summary reflects Examiner Meyers' apparent concern that "while unexpected results related to improvement of PCR by separation of targets from contaminants were relied upon in the allowance of the '338 patent, the instant specification does not make reference to PCR or to any advantage related to removal of contaminants/inhibitors." This concern appeared to be based on a belief that the unexpected results should be set forth in the specification. In the first instance, the Interview Summary correctly notes that the increased sensitivity that is achieved as a result of the combination of target capture prior to amplification is set forth in the specification. The explanation of the reasons for this increase in sensitivity is set forth in a declaration under 37 C.F.R. § 1.132 and other evidence. Indeed, a review of recent case law clarifies that the details need not be in the specification. For example, the Federal Circuit noted in *In re Chu*, 66 F.3d 292, 36 U.S.P.Q.2d, 1089, 1094 (Fed. Cir. 1995) that to do so "would be to require patent applicants to divine the rejections the PTO will proffer when patent applications are filed" and that:

> We have found no cases supporting the position that a patent applicant's evidence and/or arguments traversing a § 103 rejection must be contained within the specification. There is no logical support for such a proposition as well, given that obviousness is determined by the totality of the record including, in some instances most significantly, the evidence and arguments proffered during the give-and-take of *ex parte* patent prosecution.

Id. at 1095.

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Thus, the Patent Owner may properly rely on unexpected results, such as the removal of inhibitors of amplification, even if those results are not explicitly set forth in the specification.

2. The Broad Applicability of the Benefits of Target Capture

Examiner Meyers also inquired whether target capture provides the advantages of inhibitor removal prior to amplification for methods other than PCR. To address this point, the Patent Owner hereby submits references demonstrating that target capture provides the advantage of inhibitor removal to most amplification methods utilizing enzymes. For example, Gen-Probe suggests in their patent, U.S. Patent No. 6,130,038, which was submitted as Exhibit 7 with the original Response, that target capture prior to transcription-based amplification has the advantage of separating target nucleic acid from "substances which inhibit or interfere with the amplification reaction." Col. 18, line 50 to col. 19, line 55. The transcription-based amplification method utilizes a reverse transcriptase and T7 RNA polymerase. Col. 19, lines 22-28. (*See also* the Hill article, Exhibit 21, and Gen-Probe's Website, Exhibit 26.)

In another amplification method utilizing the enzyme Qß replicase, target capture is said to be beneficial when it precedes amplification because "the enzymatic steps (hybrid release, ligation, and amplification) are deferred until the hybrids have been isolated and placed in a defined environment; thus they cannot be inhibited by cellular components." Sanjay Tyagi et al., *Extremely Sensitive, Background-free Gene Detection Using Binary Probes and Qß Replicase*, Proc. Natl. Acad. Sci. USA, 93:5395-5400 (1996) at p. 5398, col. 1, second paragraph (attached at Tab 1). Thus, the literature

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recognizes that the benefits of target capture are not restricted to combination with PCR and, accordingly, that the unexpected results are obtained with a broad range of different amplification techniques.

Should the Examiners wonder whether or not the other discussed advantage of prior target capture, the removal of non-target nucleotide sequences, also applies to enzymatic amplification methods other than PCR, the Patent Owner refers to the same article on Qß replicase. Specifically, the Tyagi article suggests that target capture preempts "false-positive signals" that can "arise from the presence of irrelevant nucleic acids." *Id* at p. 5398, col. 1, last sentence of second paragraph. These "false-positive signals" can arise if target capture is not performed because "persistent nonhybridized binary probes on the surface of the particles are occasionally ligated to each other.... When the hybrids are isolated, the concentration of these probes is reduced to such a low level that not even a single reporter RNA is generated." *Id* at p. 5399, col. 2, first paragraph. Furthermore, in an article co-authored by Dr. Persing, it is noted that "[t]he main drawback [of the Qß replicase system] is that unbound reporter probes or nonspecifically bound reporter probes serve as templates for amplification, resulting in false-positive results. This formidable problem has been largely overcome by the use of target capture methods." Yi-Wei Tang et al., *Clinical Chemistry*, 43:11, 2021-2038 (1997) at page 2026 (attached at Tab 2).

Other benefits of target capture prior to amplification are described in another article co-authored by D. Persing:

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> Target capture may prove to be a necessary step for concentrating small numbers of target molecules from a biological fluid. For efficient recovery of *Listeria monocytogenes*, 10 ml of cerebrospinal fluid is required. *** Such large volumes are cumbersome for DNA extraction; thus a magnetic target capture system following chaotropic lysis may improve assay sensitivity and reduce sampling error. This source of error becomes important when testing small amounts of specimens that may have minute amounts of target (i.e., 1-10 molecules), because variation can occur simply from nonuniform distribution of the target throughout the sample. *** However, in combination with PCR, the capture probe sample preparation technology might be capable of detecting 10 or fewer molecules of target.

Thomas J. White et al., *Advances in Clinical Chemistry*, 29:161-196 (1992) at page 167 (attached at Tab 3).

Accordingly, there are a number of advantages to target capture prior to purification for several of the enzymatic methods of amplification encompassed by the claims.

3. The Limitations in the Kit Claims

Examiner Johannsen noted in the Interview Summary that the "kit claims would have to be examined anew, independent of the method claims" because "method step limitations cannot be read into the kit claims." Prior to that examination, the Patent Owner wishes to point out that the kit claims are comprised of means-plus-function elements.

Under 35 U.S.C. § 112, sixth paragraph, an element in a claim may be expressed as a means or step for performing a specified function without recital of structure, material, or acts that perform that function. Nonetheless, in construing the mean-plus-function language, one "must look to the specification and interpret that language in light of the corresponding structure, material, or acts described therein, and equivalents

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thereof, to the extent that the specification provides such disclosure." *In re Donaldson*, 29 U.S.P.Q.2d 1845, 1848 (Fed. Cir. 1994). *Donaldson* also emphasizes that this method of interpretation applies whether the claims are evaluated by the PTO as part of a patentability determination or by a court as part of a validity assessment. *Id.* at 1849. Thus, the means-plus-function elements of the kit claims must be interpreted in light of the specification which, in this case, is reflected by the steps in the corresponding method claims. For example, see claims 19 (a method for detecting a target polynucleotide) and 20 (a kit for detecting a target polynucleotide). Thus, while the method claims steps are not read into the means-plus-function kit claims *per se*, the methods set forth in the specification must be used to construe the kit claims.

4. The Issue of Priority

The Interview Summary notes that "the issue of priority raised in footnote 8 of the protest" is discussed in footnote 19 of the response. In reviewing the Patent Owner's Response to Gen-Probe's Protest, the Patent Owner's representative noted that the footnotes were incorrectly numbered in the Response and, accordingly, prepared and filed on January 23, 2001, a corrected copy of the Response that is identical except for the numbering of the footnotes. The corrected Response addresses Gen-Probe's priority issue at footnote 18, which explains that the priority issue had been raised by the Examiner in a continuation-in-part application of the '338 patent and that the Examiner resolved the issue in favor of the applicants.

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Finally, the Patent Owner notes with great appreciation the Examiners' recognition that the specification appears to support the amendments introduced in the reissue application and that the specification provides a basis for both specific and non-specific amplification.

Should any of the Examiners have follow-up questions, the Patent Owner requests that they contact the undersigned at (202) 408-4016 or (650) 849-6607. If there are any fees due in connection with the filing of this paper not already accounted for, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: January 31, 2001

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